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(54) **Device for the prevention of arterial restenosis.**

(57) Disclosed is a means of preventing restenosis of an artery at a trauma site due to intimal hyperplasia. That device comprises a thin wire with a radioactive tip that can temporarily be introduced into the artery and left at the trauma site for a limited period of time.

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This invention relates to devices for intra-arterial insertion that are used to maintain patency of an arterial lumen typically subsequent to balloon angioplasty or atherectomy.

Since the mid-to late 1980's, intra-arterial stents have found extensive use as a treatment to prevent restenosis subsequent to balloon angioplasty or atherectomy. A recurrent problem is that excessive tissue growth (intimal hyperplasia) at the site of the balloon dilation or atherectomy plaque excision results in restenosis of the artery. One possible solution to this problem (US Patent No. 4,768,507) is to coat the stent with an anti-thrombogenic surface so as to reduce platelet fibrin deposition. Although an anti-thrombogenic coating can prevent acute thrombotic arterial closure and decrease the need for anticoagulant drug therapy, there is still an urgent need to decrease restenosis which is caused by intimal hyperplasia.

It is well known that radiation therapy can reduce the proliferation of rapidly growing cancer cells in a malignant tumour, and this is made use in the present invention, which resides in a stent comprising a tubular structure insertable into an artery and locatable therein to maintain the lumen of the artery patent, wherein the stent comprises or is constructed of a material that is radioactive. Preferably the stent comprises a helical wire spring of the type shown in US Patent 4,768,507 and which either incorporates or is coated with a radioactive isotope, preferably a beta emitter.

Tubular radioactive structures for insertion into the body are, of course, known. For example, US-A-3,351,049 discloses a radioactive seed for radiation therapy comprising an elongate stainless steel tube, sealed at both ends and having sealed therein a radioactive source, e.g. a filamentous nylon body impregnated with a soft X-ray emitter such as I^{125}. Such seeds are simply used as a radioactive implant to be implanted in a tumour to provide a highly localised source of radioactivity.

An even more basic radioactive seed is disclosed in US-A-1954868 dating from 1929. This simply consists of a single wall capillary tube sealed at both ends and containing a quantity of radon as the radioactive source. A similar seed is shown in DE-C-867433. In this case the seed comprises a tube of a radioactive isotope sealed in a carrier tube, e.g. of Monel metal, glass, ceramic or graphite. Such devices are of little relevance to the object of the present invention, i.e. the prevention of restenosis in an artery following balloon angioplasty or atherectomy.

In the parent application (EP-A-04433011) from which the present application is divided, an intra-arterial stent is disclosed for use in the prevention of restenosis of an artery following balloon angioplasty or atherectomy and resulting from intimal hyperplasia, that stent consisting essentially of an expensible radioactive tubular structure, preferably a helical wire coil, that is insertable into the artery in a collapsed condition and which is expansible therein to bring the radioactive stent into contact with the inner surface of the artery.

The preferred form of that radioactive stent is shown in the accompanying drawings in which:

Figure 1 is a cross-section showing two turns of the radioactive helical coil spring stent embedded into a balloon dilated or atherectomized plaque within a human artery;

Figure 2 is a cross-section through the spring wire of the helical coil spring stent according to the parent application showing a radioisotope core material within the spring material;

Figure 3 is a cross-section through the spring wire of a helical coil spring stent according to the parent application showing a thin plating or radioisotope material on the exterior surface;

Figure 4 is a cross-section through a central core spring wire of a helical coil spring stent according to the parent application showing a radioisotope plating which is covered with an anti-thrombogenic coating.

Referring to the drawings, the stent comprises a radioactive helical coil spring (10) fabricated from a pure metal or alloy and coated with or incorporating a radioactive isotope and which in use is imbedded into plaque (P) within the arterial wall of the artery (AW) as is shown in Figure 1. In situ, the radioactive stent emits radiation in the direction of the arrows (12) pointing outward from the wire (10) which indicate the omnidirectional emission of particles from the stent wire. The purpose of this radiation is to decrease the rate of proliferative cell growth of the traumatized arterial wall AW (which growth is termed "intimal hyperplasia"). Thus it would be expected that restenosis, which frequently occurs after stent implantation, will be significantly reduced.

The radioisotope used for that purpose may be alpha, beta or gamma emitter. The half-life would ideally be between 10 hours and 100 days. An optimum emitter might be a beta emitting isotope such as vanadium 48 which has a half-life of 16 days and only 8% of its emitted energy is from gamma radiation. The ideal attribute of a beta emitter is that the radiation does not travel very far in human tissue. Thus only the tissue in close proximity to the radioisotope stent will be affected. Furthermore only moderate levels of radiation are desired since it is known that very high levels can cause injury to non-proliferating tissues.

Another method to make the material of the stent spring wire is from a metal into which is alloyed an element that can be made into a radioisotope. For example, phosphorus 32, a 14.3

day half-life beta emitter, could be alloyed into steel which could be used for the stent wire.

Figure 2 shows a stent wire cross-section in which a wire made from a radioisotope core material 20 is formed within an outer covering 22 that has the attributes that are desirable for being a coil spring stent.

Figure 3 shows a cross-section of an alternative embodiment in which a radioisotope coating 30 is plated onto a spring material core 32. For example, the beta emitting isotope gold 198 (half-life 2.7 days) could be used to coat any suitable spring metal material.

Figure 4 shows a more complex stent cross-section in which a core of some material ideally suited for stents is plated with a radioisotope coating 42 which is, in turn, coated with an anti-thrombogenic coating 42 such as carbon as described in US Patent No. 4,768,507.

Although helical coil spring stents have generally been described in the parent application the concept of utilizing a radioactive material within a stent structure so as to attenuate intimal hyperplasia is certainly applicable to other devices. In particular, and in accordance with the present invention, that concept is extended to a thin wire with a radioactive tip which can temporarily be placed at the site of the vessel wall trauma to prevent intimal hyperplasia and consequent restenosis of the artery, that wire being withdrawn after a limited time. Other than being a thin wire with a radioactive tip, the principle and the materials used are the same.

Claims

1. For use in the prevention of restenosis of an artery following arterial trauma, a thin wire with a radioactive tip insertable temporarily into the artery at the trauma site and serving when so inserted to prevent restenosis of the artery at the trauma site.

2. A thin wire with a radioactive tip for use in accordance with claim 1, characterised in that the wire comprises a radioisotope incorporated into the material of the wire.

3. A thin wire with a radioactive tip for use in accordance with claim 1, characterised in that the wire comprises a radioisotope plated onto the surface of the wire.

4. A thin wire with a radioactive tip for use in accordance with any one of claims 1 to 3, characterised in that the said radioisotope is a beta-particle emitter.

5. A thin wire with a radioactive tip for use in accordance with any one of claims 1 to 4, characterised in that the said radioisotope has a half-life of less than 100 days.

6. A thin wire with a radioactive tip for use in accordance with claim 5, characterised in that the radioisotope is vanadium 48 or gold 198.

7. A thin wire with a radioactive tip for use in accordance with any one of claims 1 to 6, characterised in that the wire is coated with anti-thrombogenic material.

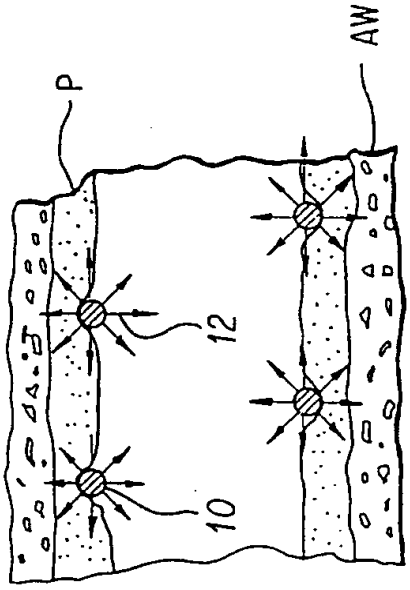

FIG. 1

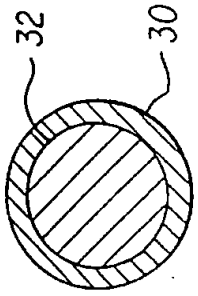

FIG. 3

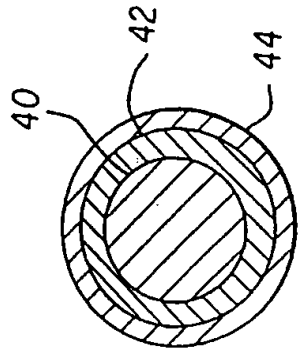

FIG. 4

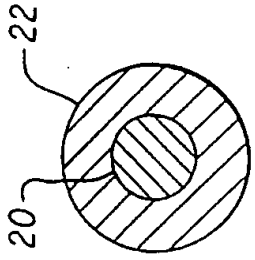

FIG. 2

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EUROPEAN SEARCH REPORT

Application Number
EP 93 20 3354

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
A	US-A-2 546 761 (LOFTUS) * claim 1; figures *	1,2	A61N5/10
A	GB-A-857 992 (BÜSCH) * page 2, line 51 - line 75; claims 1,4,5; figures *	1,2	
A	US-A-4 819 618 (LIPRIE) * claim 1; figure 7 *	1,2	
A	US-A-3 811 426 (CULVER ET AL) * column 6, line 11 - line 25; claim 1; figure *	1,3,4,7	
A	US-A-4 096 862 (DELUCA) * column 2, line 61 - line 68; figures 1,3 *	1	
			TECHNICAL FIELDS SEARCHED (Int. Cl.5)
			A61N A61M

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
BERLIN	07 JANUARY 1994	KANAL P.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
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T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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